**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**ASSAY ONLY TEMPLATE**

**A. 510(k) Number:**
k050076

**B. Purpose for Submission:**
Addition of ertapenem to the Vitek®2 Antimicrobial Susceptibility Test (AST) System

**C. Measurand:**
Ertapenem ≤0.5 – ≥ 8 µg/ml

**D. Type of Test:**
Qualitative AST growth based detection

**E. Applicant:**
bioMerieux, Inc.

**F. Proprietary and Established Names:**
VITEK®2 Gram Positive Susceptibility Card

**G. Regulatory Information:**

1. Regulation section:
   21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System

2. Classification:
   II
3. Product code:
   LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:
   83 Microbiology

**H. Intended Use:**

1. Intended use(s):
   The VITEK®2 Antimicrobial Susceptibility Test is intended to be used with the VITEK®2 System for the automated quantitative or qualitative susceptibility testing of isolated colonies for most clinically significant aerobic gram-negative bacilli, *Staphylococcus spp*., *Enterococcus spp*., *Streptococcus agalactiae*, and *S. pneumoniae*.

The VITEK®2 Gram Positive Susceptibility Card is intended for use with the VITEK®2 system in clinical laboratories as an in vitro test to determine the susceptibility of *Staphylococcus spp., Enterococcus spp.* and *S. agalactiae* to antimicrobial agents when used as instructed in the Online Product Information.

2. Indication(s) for use:
   This submission is for the addition of the antibiotic ertapenem at concentrations of 1, 2 and 4 ug/ml for a calling range of $\leq 0.5 - \geq 8$ ug/ml on the VITEK®2 Gram Positive Susceptibility Card.

3. Special conditions for use statement(s):
   For prescription use

4. Special instrument requirements:
   N/A

## I. Device Description:

Each VITEK®2 test card contains 64 microwells. A control well, that contains only microbiological culture medium is resident on all cards, with the remaining wells containing premeasured amounts of a specific antibiotic combined with culture medium. A suspension of organism is made in 0.45-0.5% sterile saline from a pure culture and standardized to a McFarland 0.5 standard using the DensiChek. The desired card(s) are placed in the cassette along with an empty tube for the susceptibility card. The cassette is placed in the VITEK®2 instrument where a susceptibility test will be automatically diluted from the ID suspension by the VITEK®2. The cards are then automatically vacuum filled; the tubes are cut and the cards sealed prior to proceeding to the Incubator Loading Station. Cards are then transferred from the cassette into the carousel for incubation (35.5$^{o}$ C) and optical scanning during testing. Readings are performed every 15 minutes.

In addition to the automatic dilution, there is also a manual inoculation dilution procedure described in the package insert.

## J. Substantial Equivalence Information:

1. Predicate device name(s):
   VITEK®2 Gram Positive Susceptibility Card for Gatifloxacin

2. Predicate 510(k) number(s):
   k032314

3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| Item | Device | Predicate |
| Intended Use | Determine antimicrobial susceptibility to antimicrobial agents | Same |
| Test Organism | Gram Positive Cocci | Same |
| Test Card | VITEK®2 card format with base broth | Same |
| Instrument | VITEK®2 System | Same |

| Differences | | |
|---|---|---|
| Item | Device | Predicate |
| Antibiotic | Ertapenem at specific concentrations | Gatifloxacin at specific concentrations |
| Reading algorithm | Unique for ertapenem | Unique for gatifloxacin |

**K. Standard/Guidance Document Referenced (if applicable):**

"Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA"; CLSI M7 (M100-S15) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard."

**L. Test Principle:**

Optics systems use visible light to directly measure organism growth. These transmittance optics are based on an initial light reading of a well before significant growth has begun. Periodic light transmittance samplings of the same well measure organism growth by how much light is prevented from going through the well. An interpretive call is made between 4 and 16 hours for a "rapid" read but may be extended to 18 hours in some instances. The VITEK®2 Susceptibility Card test is based on the microdilution minimum inhibitory concentration technique with concentrations equivalent to standard method concentrations. Several parameters based on the growth characteristics observed are used to provide appropriate input for the MIC calculations. Discriminate analysis is used to develop the algorithm that determines the susceptibility result for all antimicrobials on the VITEK®2 system. The MIC result must be linked to organism identification in order to determine a category interpretation. A category interpretation will be reported along with a MIC.

**M. Performance Characteristics (if/when applicable):**

1. <u>Analytical performance:</u>

a. *Precision/Reproducibility:*
Ten gram-positive on-scale organisms were tested three times at three sites to determine within site and site to site reproducibility demonstrating >95% reproducibility. This testing was performed using both the manual dilution of the inoculum and also the automatic dilution method.

b. *Linearity/assay reportable range:*
Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The recommended QC isolates were tested on every test occasion with the reference method and the VITEK®2. The reference method QC results were in range for every day tested. The VITEK®2 was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended range.
Quality Control was performed during the studies using both the auto-dilution and the manual method of diluting the organisms. Results demonstrated that methods were comparable with the same mode.

Quality Control Table

| ***ORGANISM*** | ***VITEK®2 Conc.*** ***(ug/mL)*** | ***VITEK®2 Auto*** | ***VITEK®2 Manual*** | ***Reference Conc.*** ***(ug/mL)*** | ***Reference*** |
|---|---|---|---|---|---|
| | | | | | |
| *S. aureus* | ≤0.5 | 73 | 66 | | 139 |
| ATCC 29213 | | | | | |
| Expected Range: | | | | | |
| 0.06 – 0.25 µg/ml | | | | | |
| | | | | | |
| *E. faecalis* | ≥8 | 72 | 66 | 8 | 84 |
| ATCC 29212 | | | | ≥16 | 54 |
| Expected Range: | | | | | |
| 4 - 16 µg/ml | | | | | |

Inoculum density control was monitored using the DensiChek instrument. This was standardized weekly with all results recorded and in the expected range. Verification was performed during internal testing.

*d. Detection limit:*
Not Applicable

*e. Analytical specificity:*
Not Applicable

*f. Assay cut-off:*
Not Applicable

2. Comparison studies:

*a. Method comparison with predicate device:*
A clinical study was conducted at three sites using the VITEK®2 gram positive cards with ertapenem and the reference agar dilution method using Mueller Hinton (MH) agar with and without 5% sheep blood prepared as recommended by CLSI. Inoculum was prepared with direct colony suspension. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. Two methods of inoculation (manual and automated) were evaluated. Clinical testing was performed using the automated method of inoculation and the challenge set was tested using both the manual and the automated method. The test device had a growth rate of >90%. All isolates grew in the VITEK®2 cards in less than 16 hours. Since Oxacillin Resistant isolates drive the call for the group, only the Oxacillin Sensitive isolates are evaluated. Essential agreement was not calculated because the VITEK®2 card contained <5 dilutions of ertapenem. A comparison was provided to the reference method with the following agreement.

Summary Table for *Staphylococcus spp.*

| | **CA Tot** | **CA N** | **CA %** | **#R** | **Min** | **maj** | **vmj** |
|---|---|---|---|---|---|---|---|
| **Clinical** | **114** | **113** | **99.1** | **1** | **0** | **0** | **1** |
| **Challenge** | **42** | **42** | **100** | **0** | **0** | **0** | **0** |
| **Combined** | **156** | **155** | **99.4** | **1** | **0** | **0** | **1** |

*Streptococcus agalactiae* is presented in the table below because it has different breakpoints than the *Staphylococcus spp*.

Also tested in the clinical study were 132 Methicillin Resistant *S. aureus* (MRSA). There were no vmj in this category. MRSAs are automatically reported as Ertapenem resistant regardless of MIC value but the ability of the VITEK®2 to detect resistance in this group accurately demonstrates that the 1 vmj for MSSA would be an acceptable error rate.

Summary Table for *Streptococcus agalactiae*

| | CA Tot | CA N | CA % | # NS |
|---|---|---|---|---|
| **Challenge** | **62** | **62** | **100** | **0** |

Only clinical isolates were tested for the *S. agalactiae* group. There are no errors possible for this group since only susceptible breakpoints exists.

**CA**-Category Agreement
**R**-resistant isolates
**NS –** Not susceptible isolates
**maj**-major discrepancies
**vmj**-very major discrepancies
**min**- minor discrepancies

CLSI's recommendation is to repeat "not susceptible" results for beta hemolytic *streptococci*.

CA is when the interpretation of the reference method agrees exactly with the interpretation of the VITEK®2 results.

Manual Dilution:
The challenge set of organisms was also tested at one site using the manual method of inoculation with the following performance that demonstrated that there was little or no difference between the two inoculation methods.

| | CA Tot | CA N | CA % | # R |
|---|---|---|---|---|
| **Challenge** | **43** | **43** | **100** | **0** |

*b. Matrix comparison:*
Not Applicable

3. Clinical studies:

*a. Clinical Sensitivity:*
Not Applicable

*b. Clinical specificity:*
Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):
Not Applicable

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:
*Staphylococcus spp.* ≤ 2 (S), 4 (I), ≥8 (R) (CLSI comment "For oxacillin resistant staphylococci, report as resistant or do not report")

*Streptococcus agalactiae* ≤ 1 (CLSI comment: "The current absence of data in resistant strains precludes defining any results other than Susceptible. Strains yielding MIC results suggestive of a "nonsusceptible" category." "Breakpoints are for reporting against beta-hemolytic streptococci only.")

The Interpretative criteria, QC isolates and the expected ranges are the same as recommended by the CLSI and the FDA. All values will be included in the package insert.

The ability of the VITEK®2 system to detect resistance to ertapenem in *S. agalactiae* organisms is unknown because resistant organisms were not available at the time of comparative testing.

**N. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**O. Conclusion:**

The submitted information in this premarket notification is complete and supports substantial equivalence decision.